ADEQ Response to AMA Comments on HAP AACs:

E^{x}ponent Technical Memorandum

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Technical Memorandum

Revised Comments on Methodology for Deriving Chronic Ambient Air Concentrations for Hazardous Air Pollutants

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Revised Comments on Methodology for Deriving Chronic Ambient Air Concentrations for Hazardous Air Pollutants

This memorandum provides refinements to Exponent's proposed methodology for deriving chronic ambient air concentrations (AACs) for hazardous air pollutants (HAPs) previously outlined in our memorandum dated October 20, 2005.

We also note that the Arizona Department of Environmental Quality's (ADEQ)'s recently released draft strawman HAPs rule incorporated two recommendations from our comments:

1. The AAC for toluene is based on the revised reference concentration (RfC), which EPA posted recently on their Integrated Risk Information System (IRIS) website
2. The risk management analysis (RMA) allows calculation of chemical-specific AACs for chemicals within compound groups, rather than using a default value based on a worst-case member of the group. We recommend that ADEQ use this more scientifically valid approach in the development of AACs in general and source category listings, not just in the case of an RMA.

Our revised methodology for deriving AACs is outlined below.

Proposed Methodology for the Derivation of Chronic Ambient Air Concentrations

We present herein a flowchart (Figure 1) for deriving chronic AACs, to illustrate a process that is more consistent with the State statute and the current weight of scientific evidence.

Step 1. Information Review

The initial step is a review of the available toxicology and epidemiology literature. A more expedient approach would be to begin with the readily available summary documents on chemicals, such as those produced by ATSDR (toxicity profiles), EPA (IRIS record, toxicological support documents), American Conference of Governmental Industrial Hygienist (documentation of TLVs), National Research Council (NRC), Health Canada, and the World Health Organization (WHO). A brief literature search may also reveal any recently published review articles. The review of this information includes identification of critical health-effect endpoints and no-observed-adverse-effect levels

(NOAELs) and lowest-observed-adverse-effect levels (LOAELs), particularly for humans, and any available toxicity values and their basis. Such values may include RfCs, URFs, or minimum risk levels and cancer effect levels derived by ATSDR, spacecraft maximum allowable concentrations (SMACs; NRC 2000), continuous exposure guideline levels (CEGLs) for submarines (NRC 2004), and threshold limit values (TLVs) of the American Conference of Governmental Industrial Hygienists (ACGIH). The latter three values (SMACs, CEGLs, and TLVs) are for astronauts, submariners, and workers, respectively. They do not include the general public and may assume shorter exposure durations; however, the documentation for these levels typically includes considerable review and evaluation of the available human toxicity and epidemiology literature and identification of NOAELs and LOAELs for various endpoints. Levels set for astronauts and submariners also assume 24-hour continuous exposures. Additional review of the database on humans is often included in the documentation of acute exposure guideline levels (AEGLs). Although these levels are set for acute exposures, the review of health effects, particularly for irritants, may also be relevant for chronic exposures.

RESPONSE: The agency considers this response to cover the entire document. This document, as well as the one submitted in October, deal with an alternative approach to the development of AACs. Several of the issues deal with the statement "significantly contribute to". It is apparent that the word significant is not defined in the statute, and Exponent has chosen to use "substantially" or "considerably", but ignores an alternative definition of "important" The agency is comfortable with its approach relating to assessment of the ability of a hazardous air pollutant to "significantly contribute to"adverse health effects.

One of the suggestions is that "An evaluation should be conducted of whether a chemical, in fact, would cause cancer to humans at low doses". It is illogical and an abrogation of the responsibility entrusted to ADEQ by the Legislature that Arizonans would end up as test subjects to prove that low doses of hazardous air pollutants will cause cancer in their population. Other issues are repeated, and the Agency's response is in the September Exponent submission (e.g., 10^{-6} risk level, background, etc.).

The recommendations included in these two documents would result in an overwhelming amount of work on each compound. Collection and review of multiple sources of data, some of which are related to healthy worker exposure, and as such, do not apply to a general population, would be enormously wasteful of government resources, and unnecessary for the intended uses of the AACs. Such an exercise would be extremely expensive and time-consuming, and in our opinion, a waste of resources when available peer-reviewed criteria have been developed that allow for a much simpler and much more effective approach. If, indeed, the Legislature had intended for ADEQ to invest the same level of effort that California and the USEPA in evaluating the health impacts of hazardous air pollutants, they would have approved the large contingent of full-time

positions and associated funding to accomplish that, which they did not.

Step 2. Exposure-Route/Data Evaluation

Once data are assembled, a key issue is the availability of inhalation-based toxicity data of sufficient quality and quantity for derivation of toxicity values. Where inhalation-based toxicity data or values are unavailable, toxicity data from other exposure routes (e.g., oral) should be critically reviewed to determine whether they could be used to evaluate toxicity by inhalation. Because of the uncertainties in extrapolating between oral and inhalation routes, EPA has advised considerable caution with such extrapolations (see previous comments), and some state air programs (e.g., Texas) have advised against such extrapolations (TNRCC 1999). In addition, the EPA Office of Air Quality Planning and Standards discussion on application of risk assessments of hazardous air pollutants states: "We do not recommend oral-to-inhalation conversion for assessments that may lead to regulatory actions."

Review of Table 1 in the Chronic AAC document indicates that the toxicity values for a number of the chronic AACs are based on extrapolation from oral toxicity studies.[1] We also note that even when a slope factor or URF, for example, is listed by EPA (e.g., in PRG tables) as an inhalation value, this value could have been derived from an oral study in some cases (e.g., chloroform, TCE). Although disregarding the route of exposure results in more available toxicity values, application of toxicity values based on the oral route of administration is highly uncertain and may not be representative of inhalation risks. As stated previously, toxicity criteria based on extrapolation from oral studies should not be used to derive AACs, unless such an extrapolation can be scientifically justified. The appropriateness of carrying out route-to-route extrapolation should be determined on a case-by-case basis and must account for the relationship between physicochemical properties, the absorption and distribution of toxicants, the significance of portal-of-entry effects, and the potential differences in metabolic pathways associated with the intensity and duration of exposure. Other toxicity information, such as human inhalation exposure studies, should also be considered as an alternative to route-to-route extrapolation.[2]

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1 Examples include acetophenone, antimony compounds, benzyl chloride, bisphenyl, bis (2-ethylhexyl) phthalate, bromoform, chloroform, dibenzofurans, N,N-dimethylaniline, 2,4-dinitrotoluene, ethylene dichloride, hexachlorobenzene, polychlorinated biphenyls, selenium compounds, 1,1,2,2-tetrachloroethane, and trichloroethylene. (This list has been corrected from our September 8, 2005 comments. Other oral-to-inhalation extrapolations may also be found if the basis of the AAC for each chemical in the chronic AAC document were investigated.)

2 We note that ADEQ's chronic AAC for ethylene glycol was derived from a value based on inhalation studies in humans, rather than a value based on oral feeding study in rats. We agree with this selection, although under our proposed methodology, the derivation of the selected value should also be evaluated (e.g., quality of study, endpoint, uncertainty factors).

If the available scientific data are insufficient to derive an inhalation value, the AAC should not be derived. Instead, a qualitative evaluation should be performed with the chemical being set aside as needing more information for AAC development.

Step 3. Toxicity Value Evaluation and Adjustment

Once potential toxicity values or data that can be used to represent inhalation toxicity are assembled, their scientific basis should be reviewed:

1. Identify data and toxicity values for critical low-dose endpoints that are consistent with the definition of adverse effects according to the Arizona State statute (i.e., those that "result in or significantly contribute to an increase in mortality or an increase in serious irreversible or incapacitating reversible illness, including adverse effects that are known to be or may reasonably be anticipated to be caused…)."

2. Evaluate the weight of evidence for each value: quality of study(ies) used to derive value, human vs. animal, mechanistic considerations, justification for uncertainty factors. The objective of this step is to identify the data with the strongest technical basis.

3. Once the weight-of-evidence step is completed, data should be reviewed to consider whether an adjustment (up or down) is needed to better represent the applicable exposure setting and consistency with the statute. In addition, some adjustment may be needed to be consistent with reasonable maximum exposure assumptions (such as used in ADEQ's Chronic AAC document) or with the State statute. If an occupational-based toxicity value is identified (assuming that it is health-based) as an appropriate value, it may need to be adjusted to be protective of residential exposures. Any adjustments, however, should consider the underlying scientific data for specific chemicals in deciding the magnitude of such factors. For example, the toxicity of some chemicals may be more concentration dependent than time dependent and would not require large time adjustment factors (e.g., some irritants). Other chemicals may have robust data that indicate that the species tested was relatively more or less sensitive compared to humans, or that there is more or less variation in the human population for a certain endpoint. The EPA and various NRC committees currently incorporate such information in setting the magnitude of uncertainty factors, rather than using default factors of 10 for each source of uncertainty. Scientific data have indicated that a full factor of 10 is conservative for most sources of uncertainty, particularly for chemicals with a relatively complete database to assess such uncertainty (Dourson et al. 1996).

4. An evaluation should be conducted of whether a chemical, in fact,

would cause cancer to humans at low doses. Information to consider includes epidemiological data, the nature of the tumors reported in animal studies, consistency among species and sexes, and mechanistic and genotoxicity evidence. If a full assessment is too onerous, then at a minimum, the evidence from recent reviews of other scientific panels and literature reviews should be considered. For those chemicals for which cancer at low doses cannot be ruled out, the URF should be adjusted to also consider an air concentration at a 10^{-4} risk level. This level is the upper limit of the typical acceptable risk range and is still well below risks that could actually be detected in a population, and thus is more in line with the statute's language. It should be recognized that this risk level still contains a considerable margin of safety because of the assumption of no-threshold, linear extrapolation of risk from high doses combined with worst-case exposure assumptions.

Step 4. Select AAC

The final step involves the selection of the AAC value. Of the data available to derive an inhalation AAC, the selection should focus on the critical endpoints at lower doses that are consistent with screening out levels that would "result in or significantly contribute to an increase in mortality or increase in serious irreversible or incapacitating reversible illness." If more than one value is well supported by the scientific evidence, the lowest value consistent with the statute language should be selected.

For some chemicals, it is possible that even a complete evaluation may result in a value for which considerable uncertainty adjustments are necessary, thereby potentially magnifying overestimation of toxicity and reducing the value for identifying exposures that would result in adverse effects, as defined by the statute. Thus, comparison to typical ambient levels is a means of ensuring that the resulting levels include some perspective from practical experience. The resulting toxicity value should be compared with available data for typical ambient (e.g., annual) non-point-source concentrations for the chemical. The resulting AAC should not be set lower than typical ambient concentrations that have been found to be well tolerated by humans with no consistent evidence of adverse effects.

References

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